ELECTION

In response, Applicants hereby elect **Group I**, Claims 1-14, *with traverse*, for prosecution on the merits. However, Applicant hereby respectfully requests that the Examiner reconsider and withdraw the restriction requirement between the inventions of Groups I, II, and III, for reasons provided below. A copy of the pending claims is attached as Appendix A, entitled "Clean Pending Claims."

REMARKS

I. Restriction Requirements: When Proper

Restriction requirements are proper only when the inventions are independent or distinct, and examination without restriction presents a serious burden to the examiner. See MPEP § 803. Examiners must provide reasons and/or examples to support their conclusions regarding the status of the inventions and the seriousness of the burden. Id. If the search and examination of the application can be made without serious burden, the Examiner must examine the subject application on the merits even if includes claims to distinct inventions. Id.

II. Inventions of Groups I, II and III are Related and Should Not be Restricted

The Examiner argues that the inventions of Groups I, II and III are distinct because they are unreleated.

Inventions are unrelated if it can be shown that there is no disclosed relationship between them, i.e., if they are unconnected in design, operation or effect.[1] The Examiner argues that the inventions of Groups I, II and III are unrelated because "the different inventions are different methods with different method steps where each method results in different ends." See Office Action at 2.

Applicants respectfully disagree with the Examiner's characterization of the inventions of Groups I, II and III as unrelated. Each of the inventions in Groups I, II and III are connected in design because the inventions in these groups involves a composition or method relating to the modulation of VEGF activity.

In addition, the Examiner will search identical or largely overlapping subject areas when conducting prior art searches with respect to the groups identified by the Examiner. Applicant respectfully submits that the redundant searching required will not constitute a "serious burden" for the Examiner.

For all the forgoing reasons, the Examiner is respectfully requested to reconsider and withdraw the requirement for restriction between Groups I, II, and III. An action on the merits of these elected claims and a Notice of Allowance thereof are respectfully requested.

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[1] See MPEP § 806.04, MPEP § 808.01. Note that a finding of unrelatedness is akin to a finding of "independence." In contrast, a finding of "distinctness" generally assumes that the inventions *are* related. See MPEP 806.05.

If the Examiner has any questions concerning this Response, the Examiner is respectfully requested to telephone Applicants' agent at the following telephone number (415) 393-2778.

NOTICE OF FIRM NAME CHANGE

Agent for Applicant wishes to inform the Office that the name of its firm has been changed to Bingham McCutchen LLP.

DATE: 11/19/2002

Respectfully submitted,

By: _____
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Appendix A: Clean Pending Claims

1. A composition comprising an antisense oligonucleotides directed against vascular endothelial growth factor (VEGF), wherein said antisense oligonucleotide is UGGCTTGAAGATGTACTCGAU (SEQ ID NO: 34).

2. The composition of Claim 1 further comprising another active agent.

3. The composition of Claim 2 wherein said active agent is a chemotherapeutic such as Taxol.

4. The composition of Claim 1 further comprising one or more antisense oligonucleotides antisense oligonucleotides directed against vascular endothelial growth factor (VEGF) and which inhibit the proliferation of cells exhibiting autocrine VEGF activity at an IC_{50} concentration of between about 0.5 to about 2.5 micromolar.

5. The composition of Claim 4, wherein the IC_{50} concentration is less than or equal to about 1.5 micromolar.

6. The composition of Claim 5 wherein said antisense oligonucleotide inhibits proliferation of cultured melanoma cells at an IC_{50} concentration of less than or equal to about one micromolar.

7. The composition of Claim 4 wherein said cells are ovarian cancer cells, melanoma cells, Kaposi's sarcoma cells prostate cells or pancreatic cancer cells.

8. An antisense oligonucleotide having the sequence UGGCTTGAAGATGTACTCGAU (SEQ ID NO: 34).

9. A method for inhibiting cancer cell proliferation or angiogenesis comprising comprising contacting said cell with an antisense oligonucleotides directed against vascular endothelial growth factor (VEGF), wherein said antisense oligonucleotide is UGGCTTGAAGATGTACTCGAU (SEQ ID NO: 34).

10. The method of Claim 9, wherein said cell is an ovarian cancer cells, melanoma cells, Kaposi's sarcoma cells prostate cells or pancreatic cancer cell.

11. The method of Claim 9, further comprising contacting the cancer cell with one or more antisense oligonucleotides directed against vascular endothelial growth factor (VEGF) wherein said antisense oligonucleotide inhibits proliferation of cells exhibiting autocrine VEGF activity at an IC_{50} concentration of between about 0.5 to about 2.5 micromolar.

12. The method of Claim 11, wherein the the IC_{50} concentration is less than or equal to about 1.5 micromolar.

13. The composition of Claim 12 wherein the IC_{50} concentration is of less than or equal to about one micromolar.

14. The method of Claim 9 wherein said antisense oligonucleotide is encapsulated in a liposome.

15. A method of assessing the therapeutic potential of a candidate agent to inhibit cancer cell proliferation or angiogenesis, said method comprising: (i) contacting cells exhibiting autocrine growth activity with at least one candidate and (ii) measuring the level of VEGF expression or activity or cell growth, wherein an inhibition in VEGF expression or cell growth is indicative of the candidate agent's therapeutic potential.

16. The method of Claim 15, wherein said cells are Karposi's sarcoma cells, ovarian cancer cells, prostate cancer cells, pancreatic cancer cells or melanoma cells.

17. The method of Claim 16, wherein said candidate agent is an antisense oligonucleotide.

18. A a prognostic assay for a subject afflicted with a disease involving abnormal cellular proliferation or angiogenesis, comprising::

(i) isolating a biological sample a subject afflicted with a disease involving abnormal cellular proliferation (e.g., cancer) or angiogenesis; and (ii) evaluating said sample for autocrine

VEGF activity or VEGF expression or VEGF receptor expression, wherein autocrine activity is indicative of a poorer prognosis for said subject.